

Figure 1

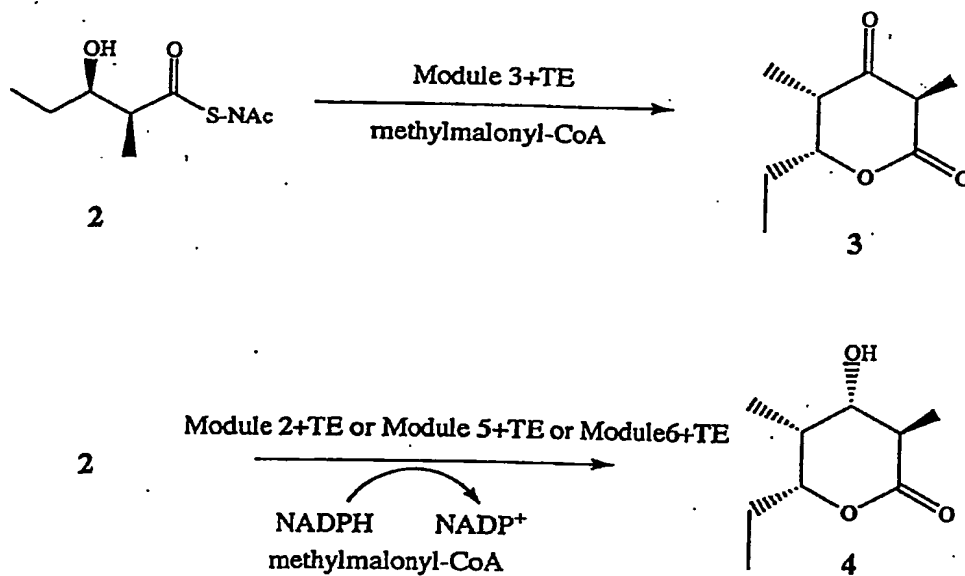


Figure 2

(a) INTRA-POLYPEPTIDE LINKER

M2ery: GGATGAEQAAPATT..APVD
M4ery: VGDAĐ..QAA.VRVVGAA.DES
M6ery: VGAAEAEQA.PALVREVPKDAD
M2rif: FGSA.A.NR.PAEIGTAAAE
M3rif: LG..ER.PAAPAPVTRDVSD
M5rif: GETVAGAPATPVTTVADAG
M3rap: .ELFTGENPAPVRGPVSAVGQD
M4rap: .ELFTGENPAPVRGPVSVVGQD
M7rap: .ELFTGENPAPVRGPVSA.GQD

(b) N-TERMINAL INTER-POLYPEPTIDE LINKER

M3ery:VTD SE KVAEYLRR .ATLĐLRAAR QRIRE..LES
M5ery: MSGDNGM.TE E.KLRRYLKR TVT.ELDSVT ARLRE..VEH RAG
M4rif:MSAPNE QIVDAL.R ASLKE....N VRLQOENSAL AAAAA
M7rif:VSASYE KVVEAL.R KSLEE....V GTLKKRNRQL ADAAG
M8rif:V.AD EGQLRDYLKR .AIADARDAR TRLRE..VEE QAR
M9rif:MATD E.KLLKYŁKR .VTAEŁHS.. ..LRKQGARH .AD
M5rap:MR.. EDQLLDAL.R KSVKE....N ARLRKANTSL RAAMD
M11rap:M.PEQD KVVEYL.R WATAELHTTR AKL.....EA LAAANT

Figure 3

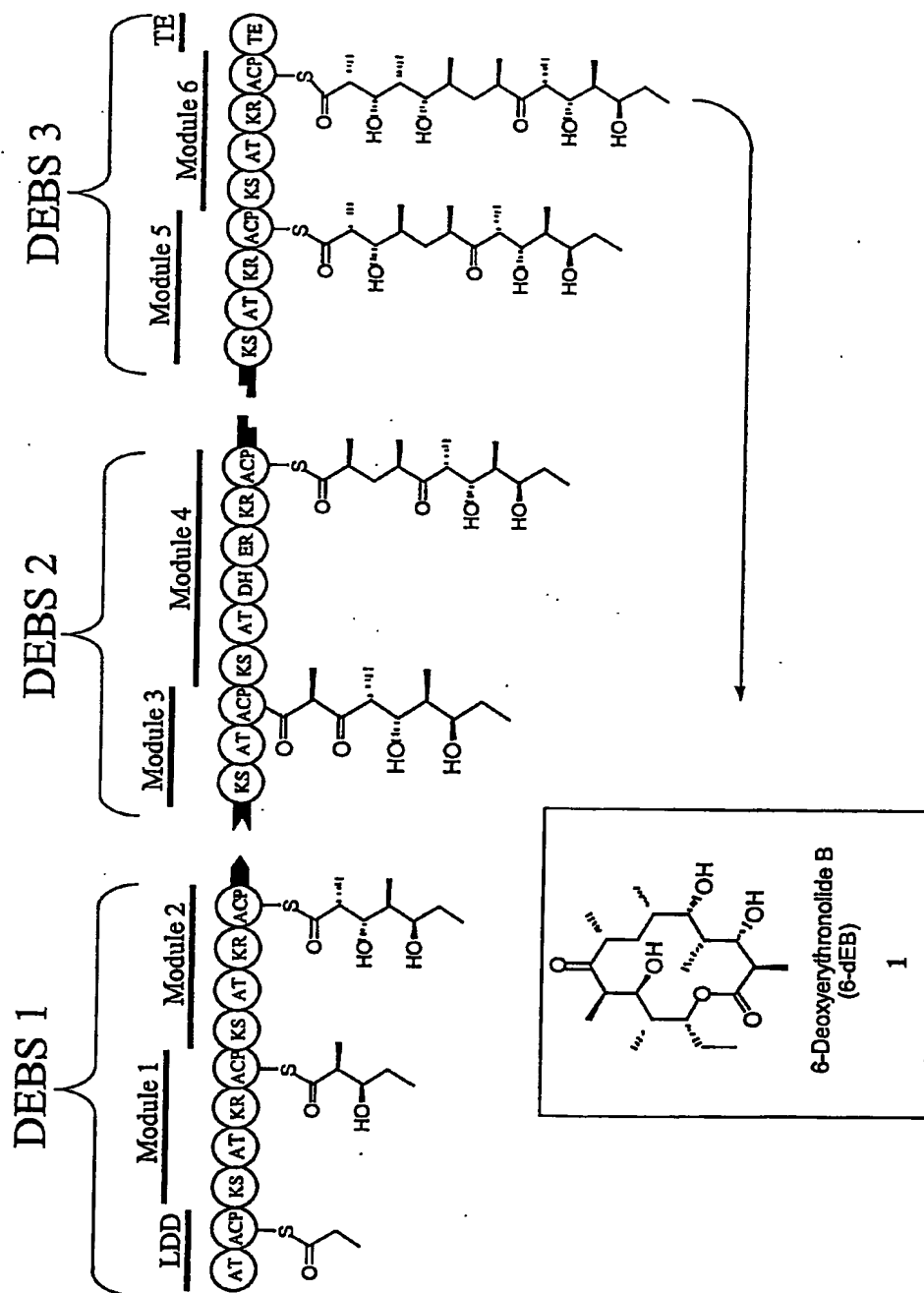


Figure 4

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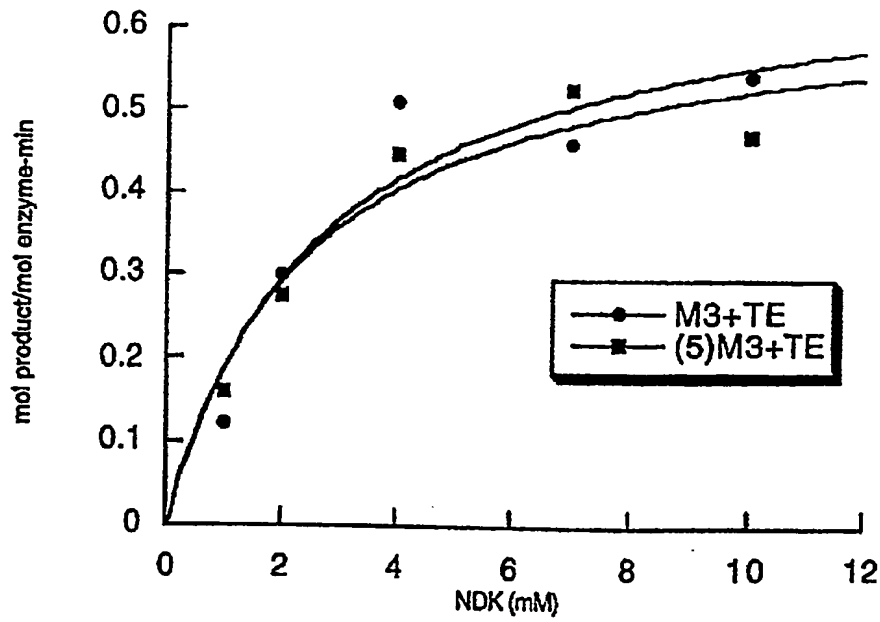
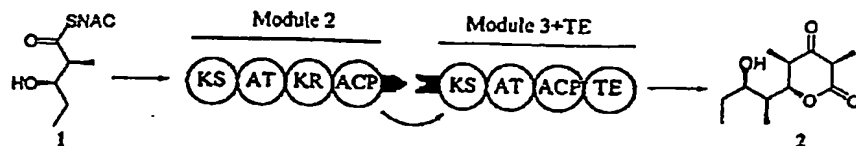
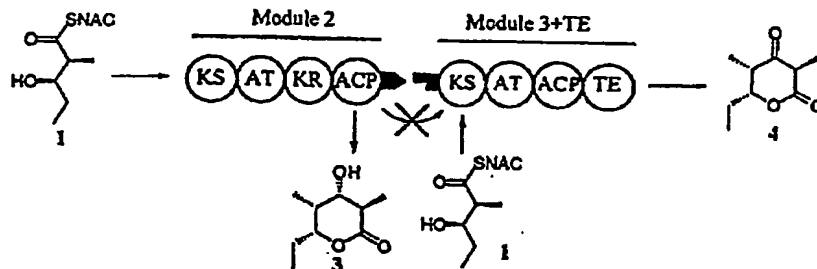


Figure 5

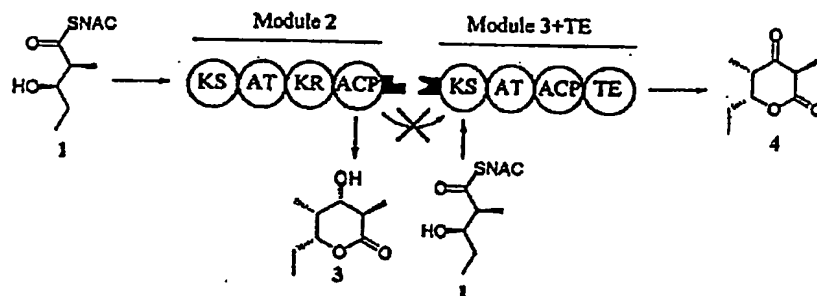
A. M2 and M3+TE



B. M2 and (5)M3+TE



C. M2(4) and M3+TE



D. M2(4) and (5)M3+TE

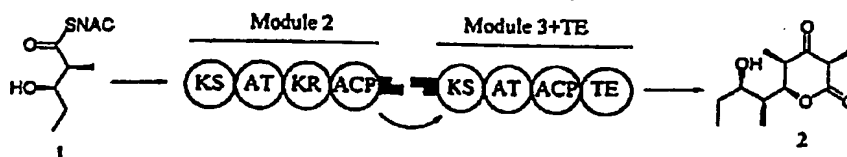


Figure 6

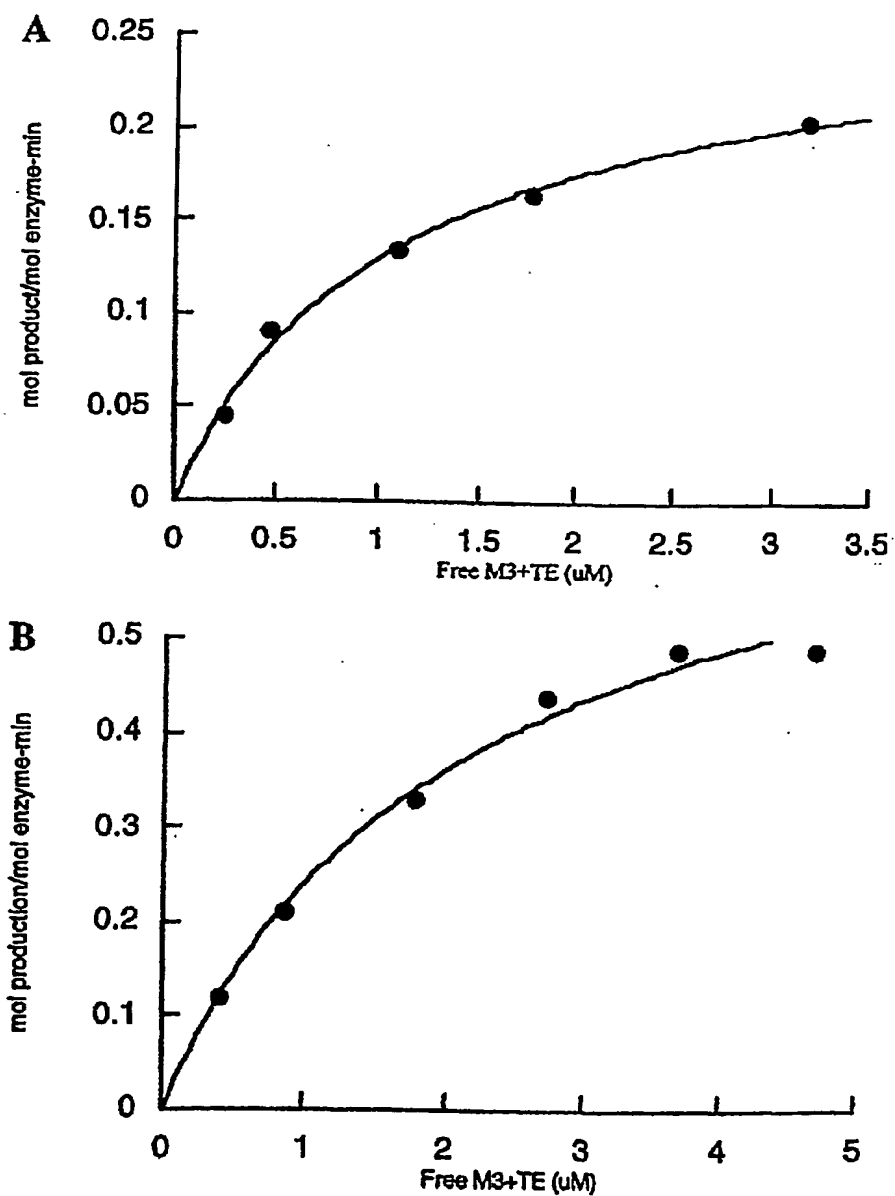


Figure 7

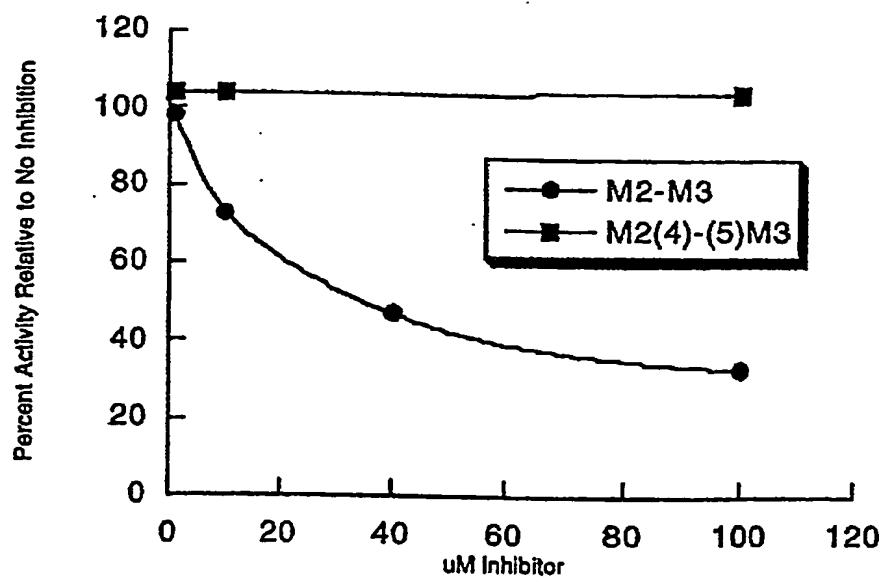


Figure 8

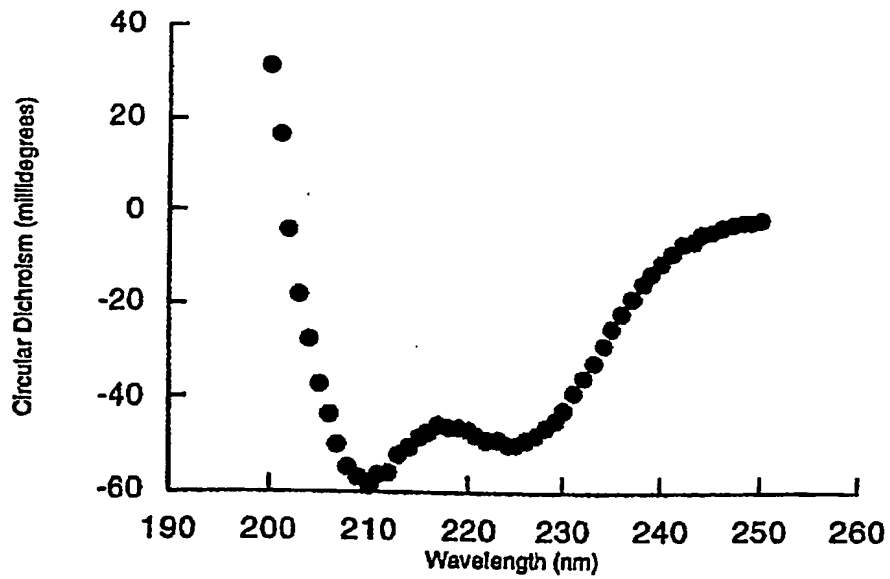
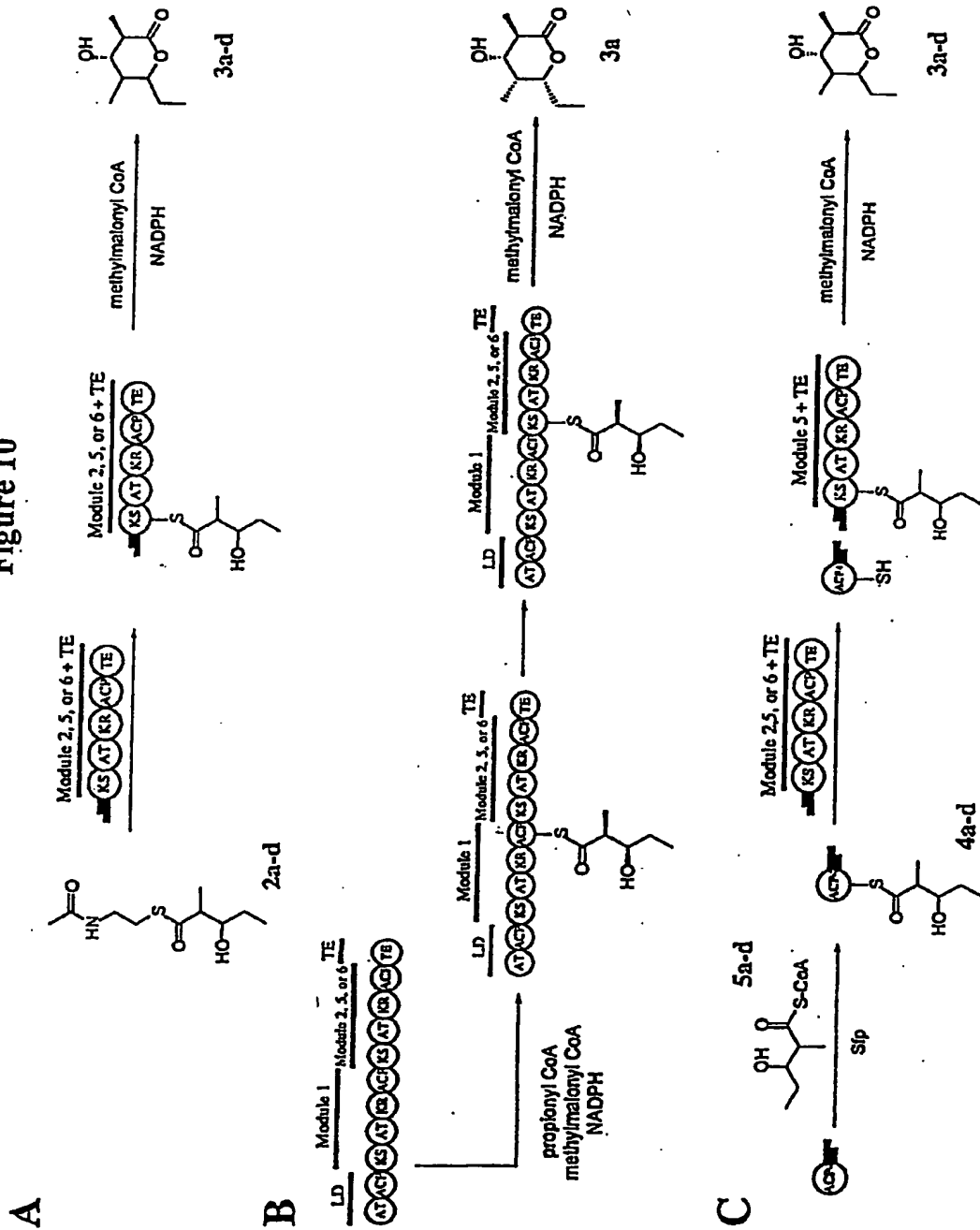


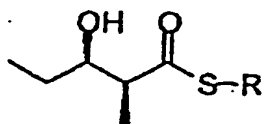
Figure 9

Figure 10

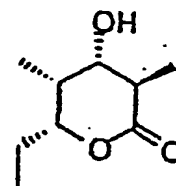


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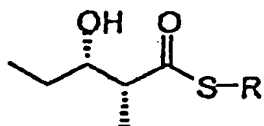
PCT/US03/06910



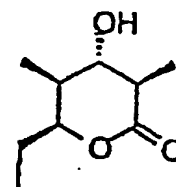
2a: R=N-acetylcysteamine
4a: R=Acyl carrier protein



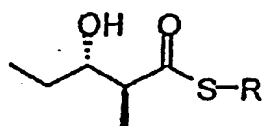
3a



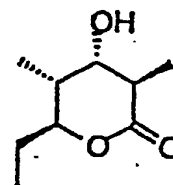
2b: R=N-acetylcysteamine
4b: R=Acyl carrier protein



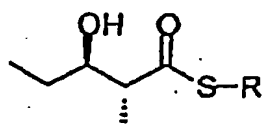
3b



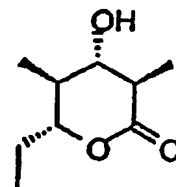
2c: R=N-acetylcysteamine
4c: R=Acyl carrier protein



3c



2d: R=N-acetylcysteamine
4d: R=Acyl carrier protein



3d

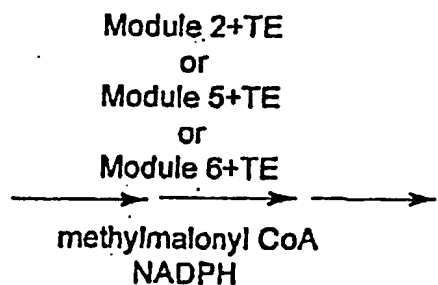


Figure 11

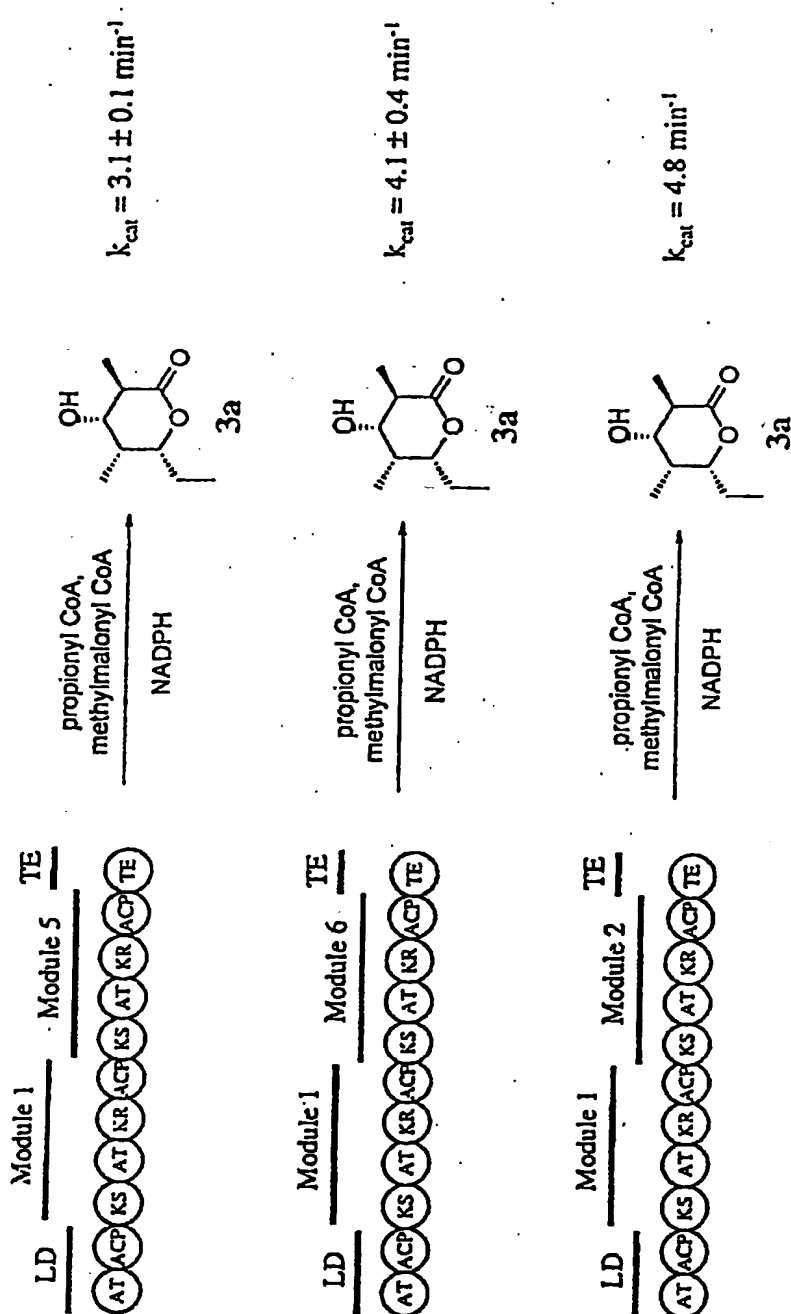


Figure 12




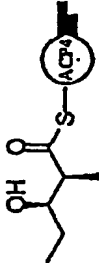
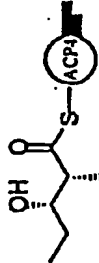
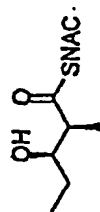
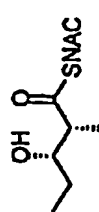
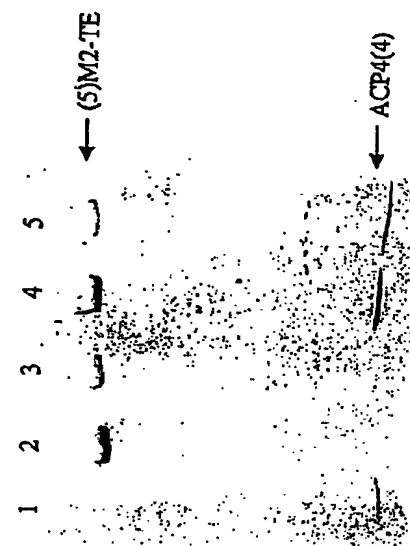
Substrate	(5)Module 2 + TE 	(5)Module 5 + TE 	(5)Module 6 + TE 
4a 	2900 ± 500	290 ± 50	340 ± 60
4b 	18 ± 1	3.9 ± 0.7	85 ± 15
2a 	0.75 ± 0.01	0.016 ± 0.002	1.1 ± 0.1
2b 	0.0076 ± 0.0006	0.0011 ± 0.0001	0.058 ± 0.006

Figure 13

Substrate	(S)Module 2 + TE	(S)Module 5 + TE	(S)Module 6 + TE
	KS AT KR ACP TE	KS AT KR ACP TE	KS AT KR ACP TE
4a 	6.7 ± 0.2	> 9.3 ± 1.4	> 10 ± 1
4b 	> 0.97 ± 0.02	> 0.48 ± 0.02	> 3.4 ± 0.4
4c 	> 1.0 ± 0.1	> 1.4 ± 0.1	> 2.1 ± 0.2
4d 	> 0.29 ± 0.03	> 0.20 ± 0.01	> 1.9 ± 0.1
2a 	> 4.6 ± 0.6	0.24 ± 0.01	17 ± 2.9
2b 	0.25 ± 0.02	0.017 ± 0.001	2.4 ± 0.2
2c 	N.D.	N.D.	N.D.
2d 	N.D.	N.D.	N.D.

Figure 14



Lane	ACP	Module	¹⁴ C-Label	Extender	Unit
1	holo-ACP4(4)	none	* 2 a	none	
2	none	(5)M2+TE	* 2 a	none	
3	none	(5)M2+TE	* 2 a	methylmalonyl-CoA	
4	holo-ACP4(4)	(5)M2+TE	* 2 a	none	
5	holo-ACP4(4)	(5)M2+TE	* 2 a	methylmalonyl-CoA	

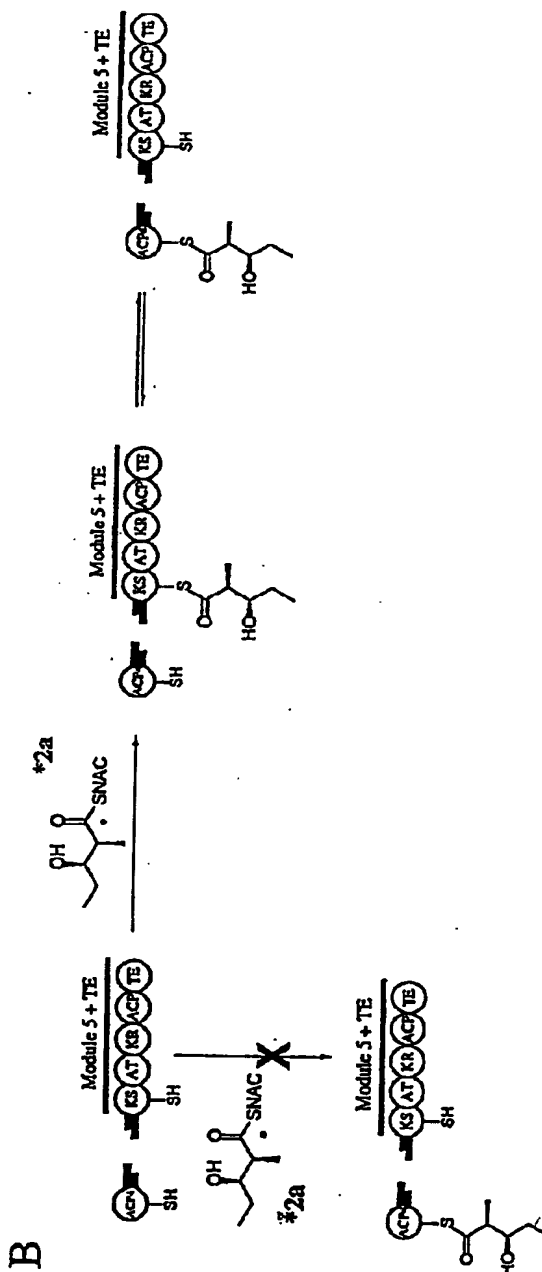
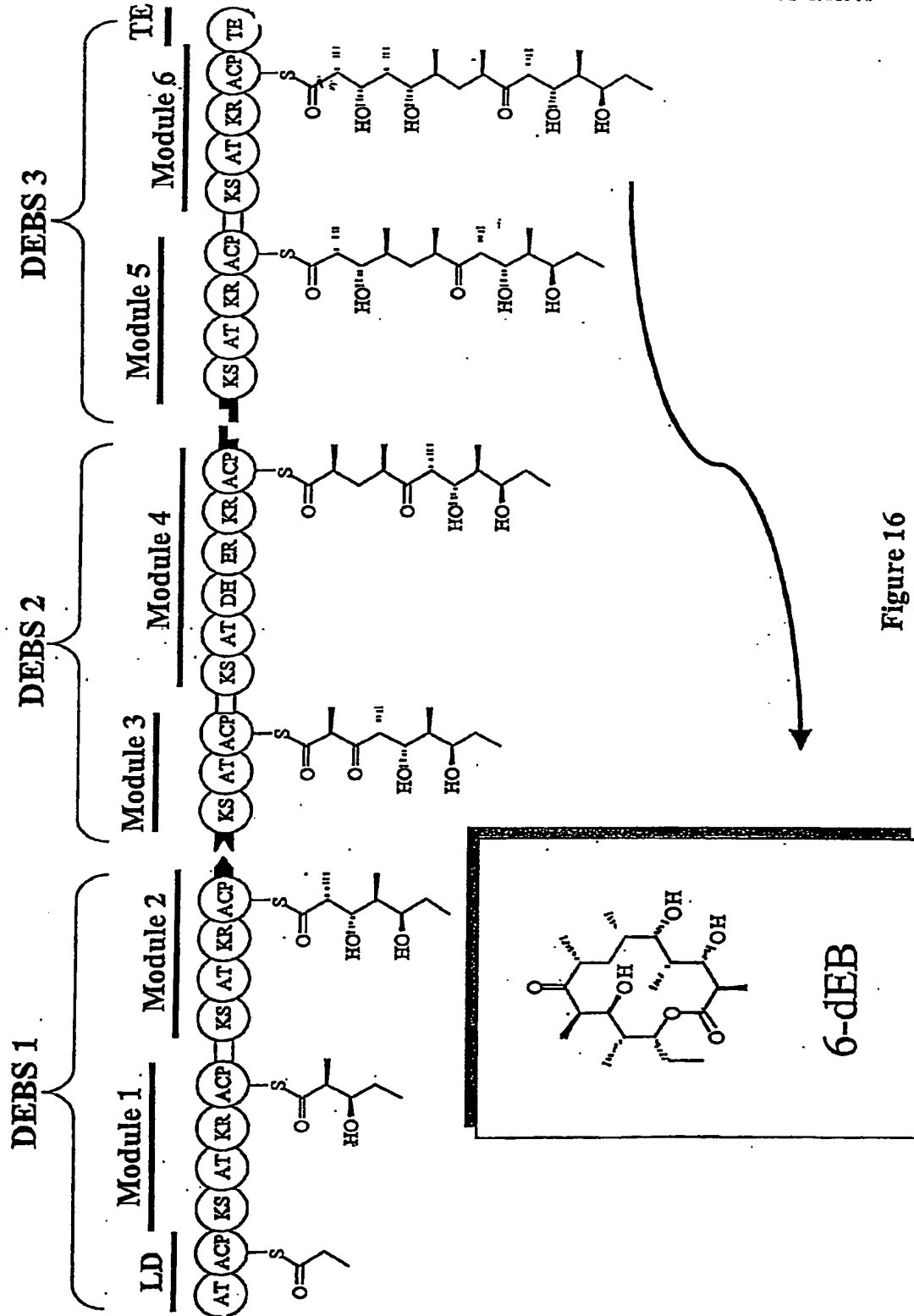


Figure 15



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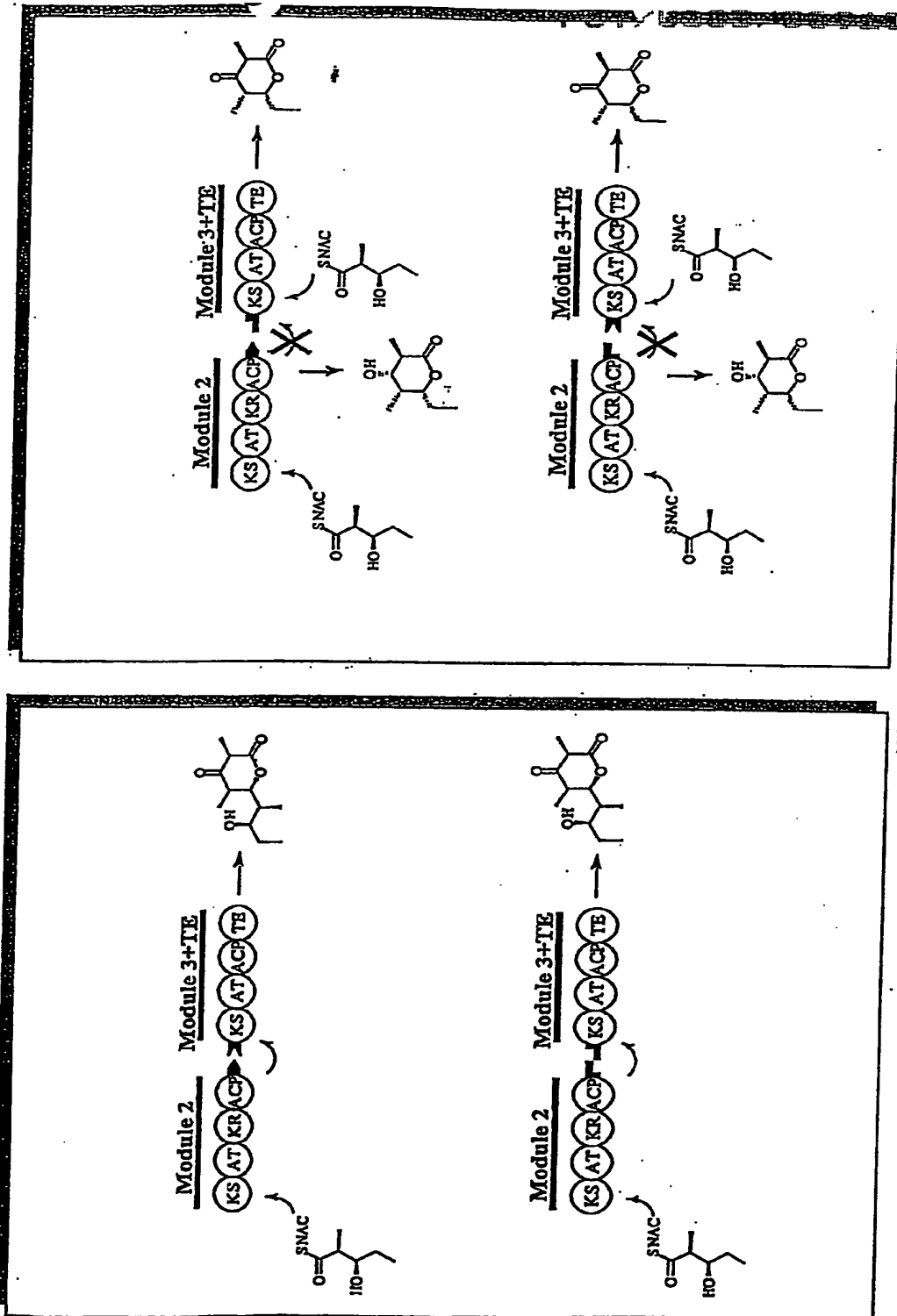


Figure 17

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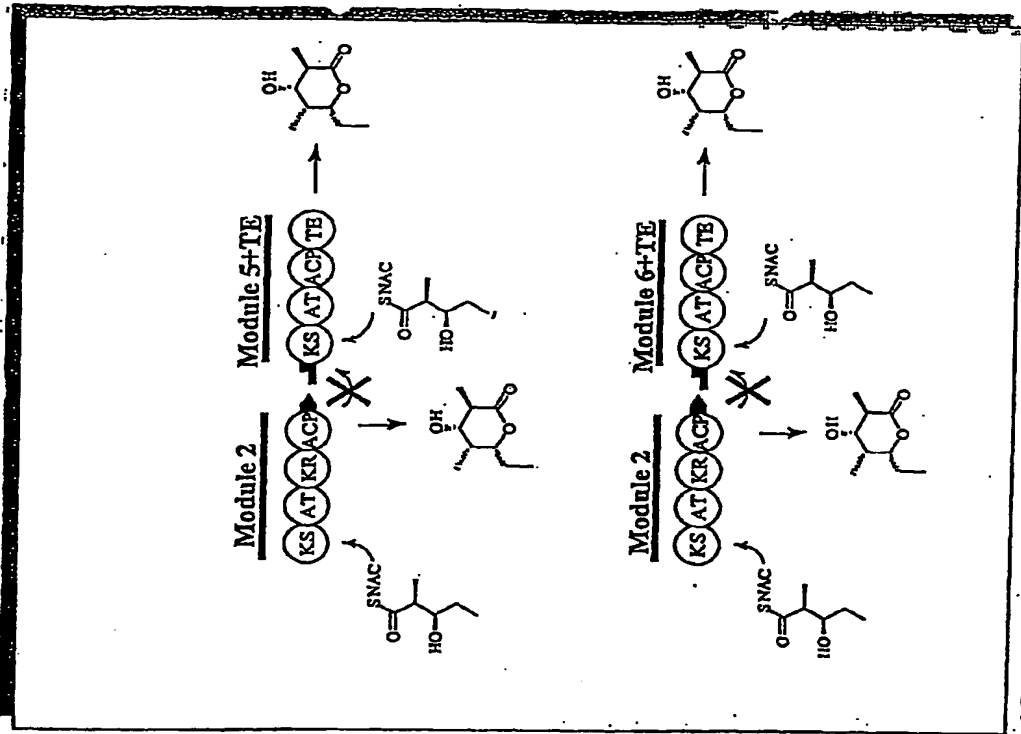
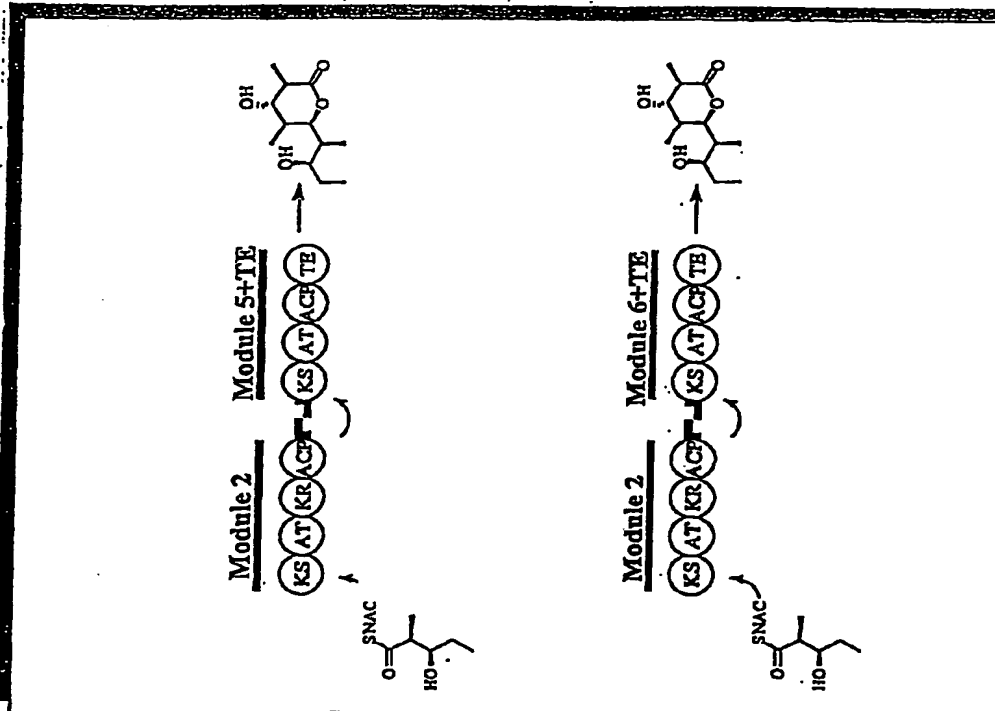


Figure 18



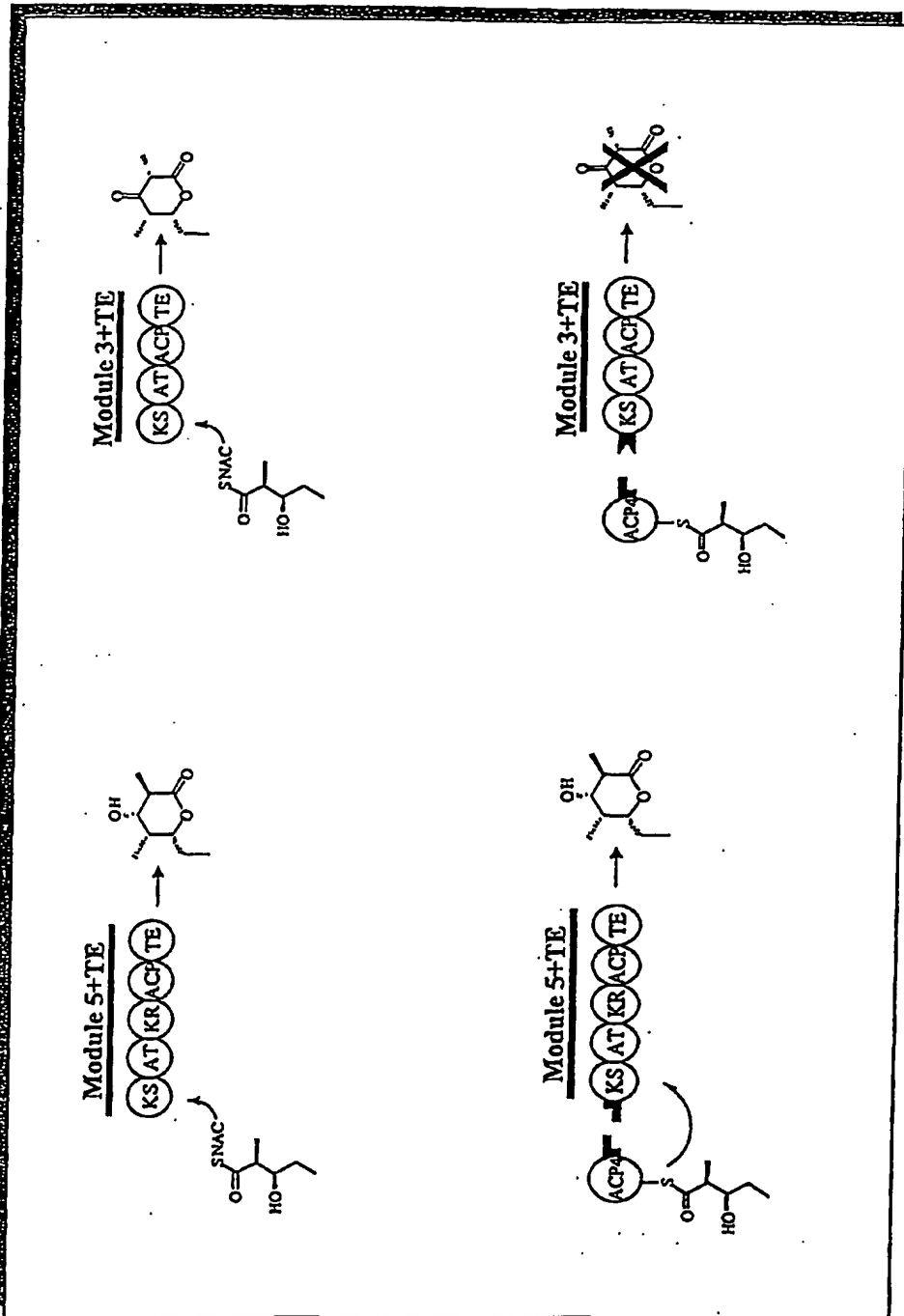
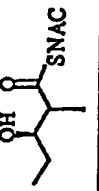
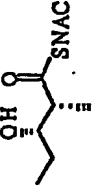
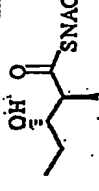
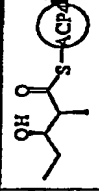
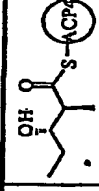
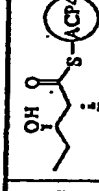
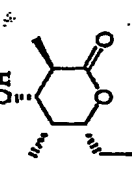
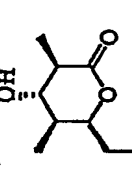

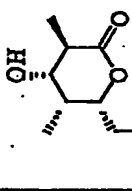
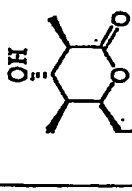
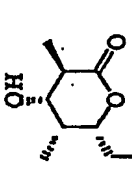
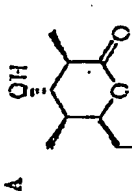

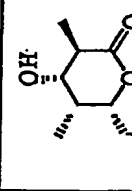
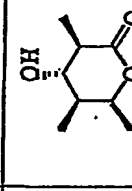


Figure 19

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Figure 20

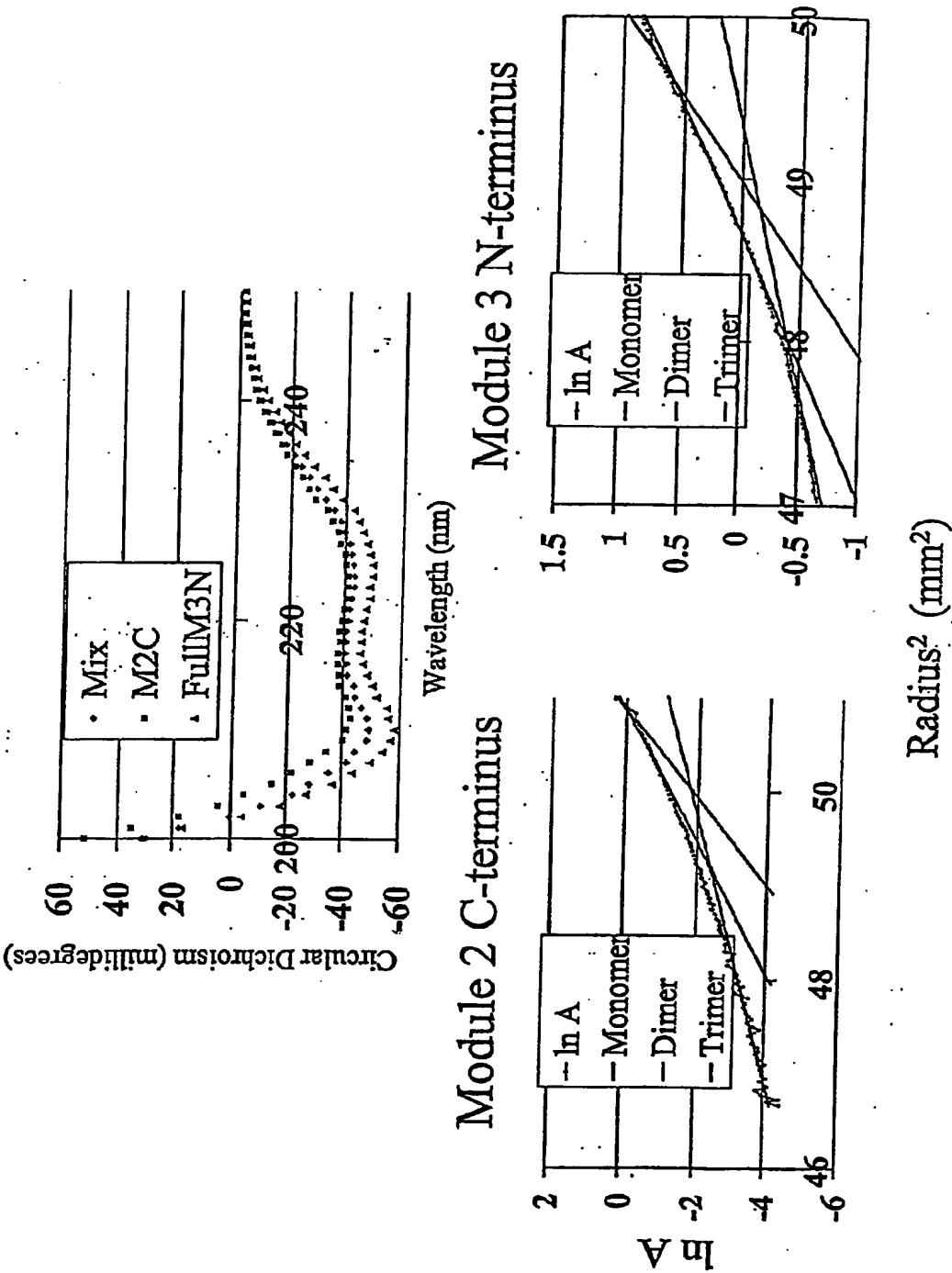
Substrates Enzyme						
Module 2 + TE KS AT KR AC TE			X			
Module 5 + TE KS AT KR AC TE			X			

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Figure 21

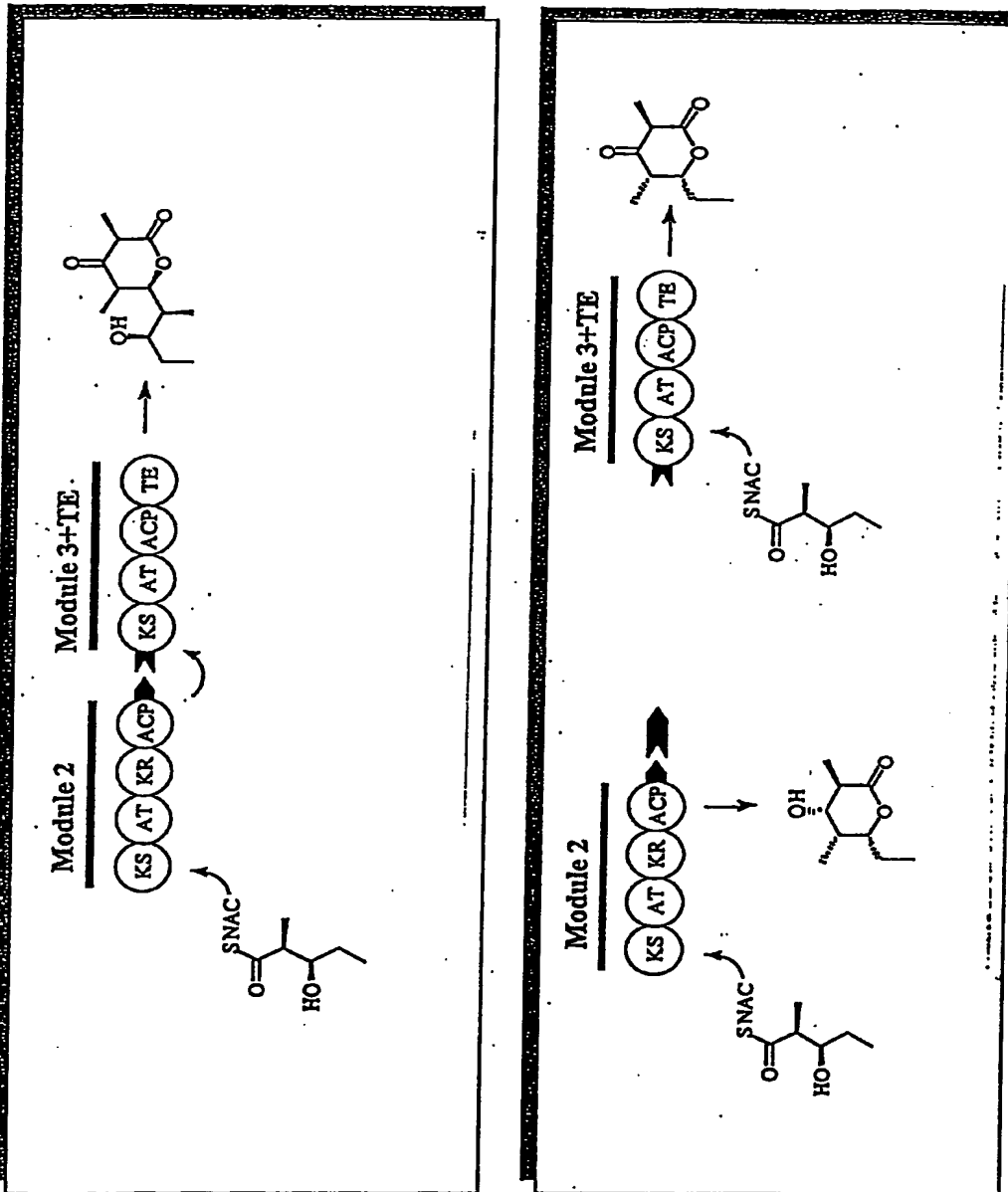


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Figure 22



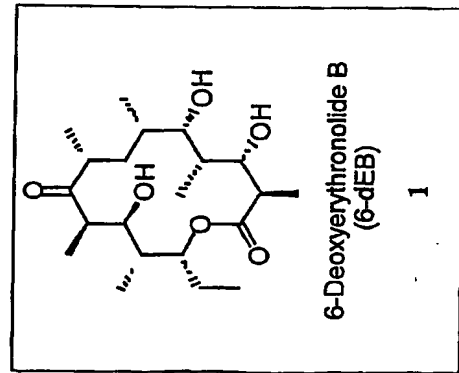


Figure 23

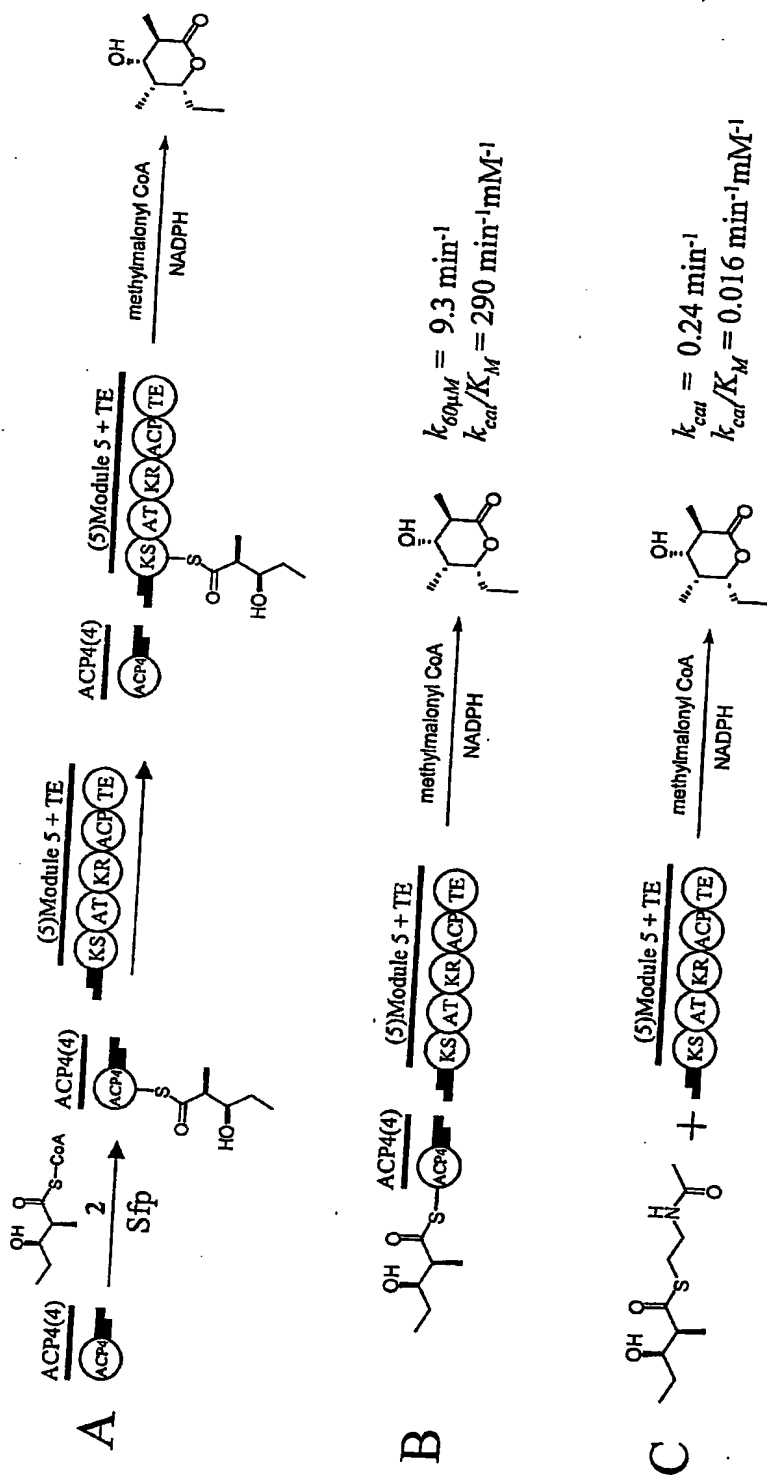


Figure 24

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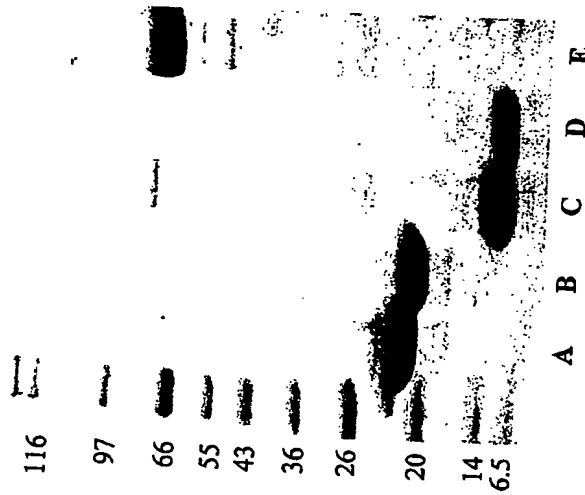


Figure 25

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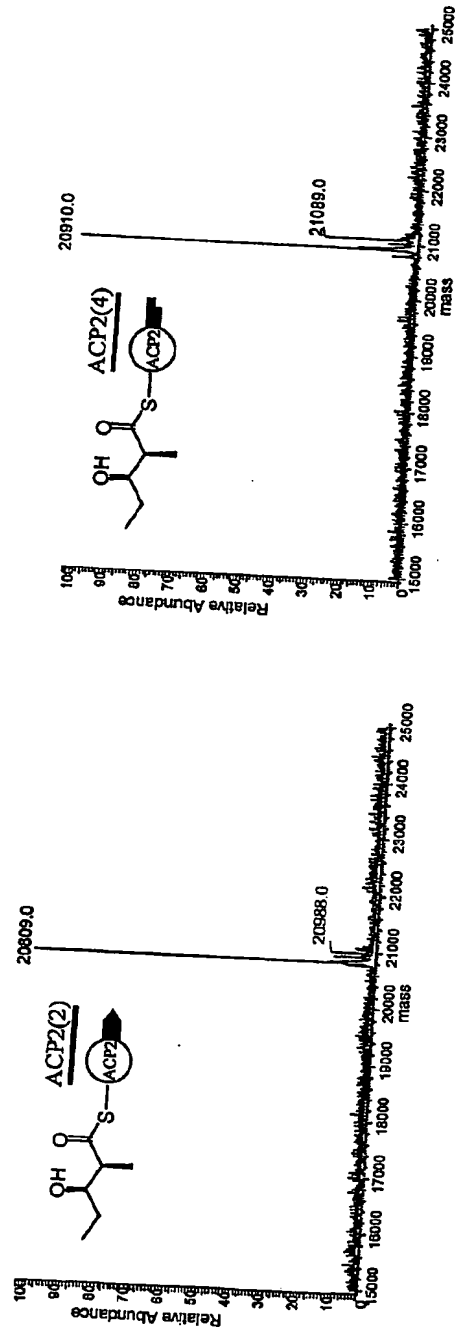
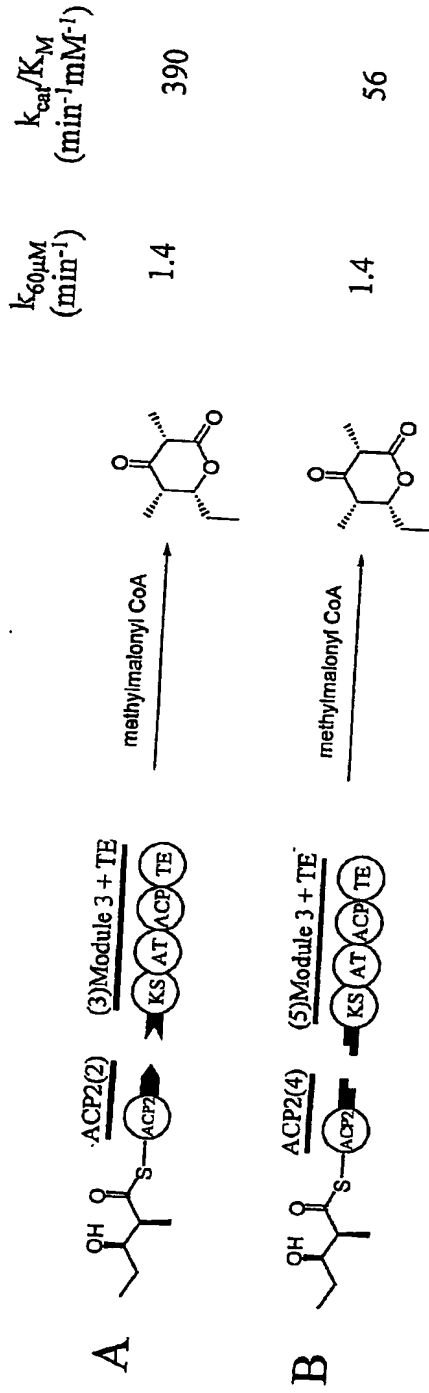


Figure 26

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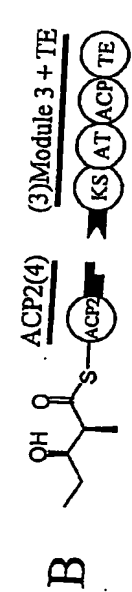
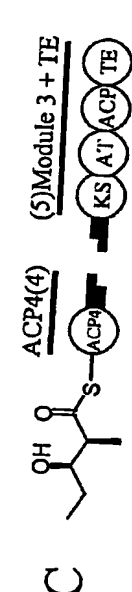
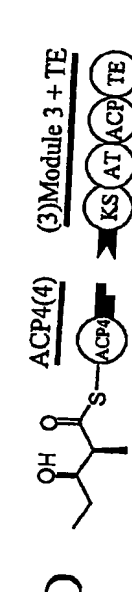
k_{cat}/K_M ($\text{min}^{-1}\text{mM}^{-1}$)	$k_{50\mu\text{M}}$ (min^{-1})	
390	1.4	
6.5	0.52	
2.0	0.33	
N.D.	N.D.	

Figure 27

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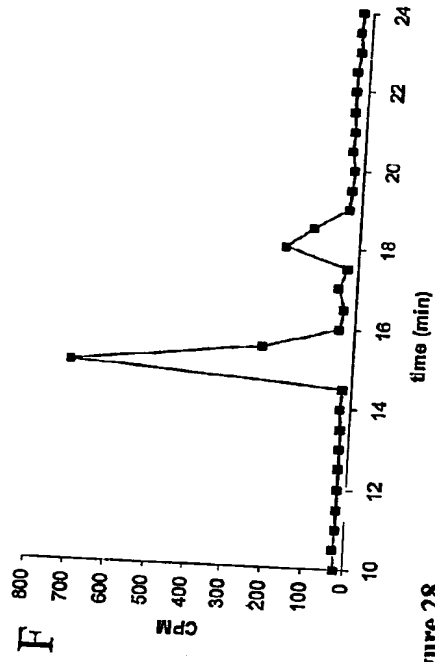
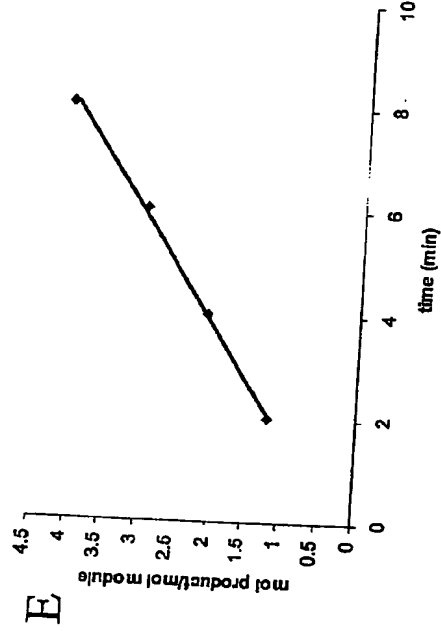
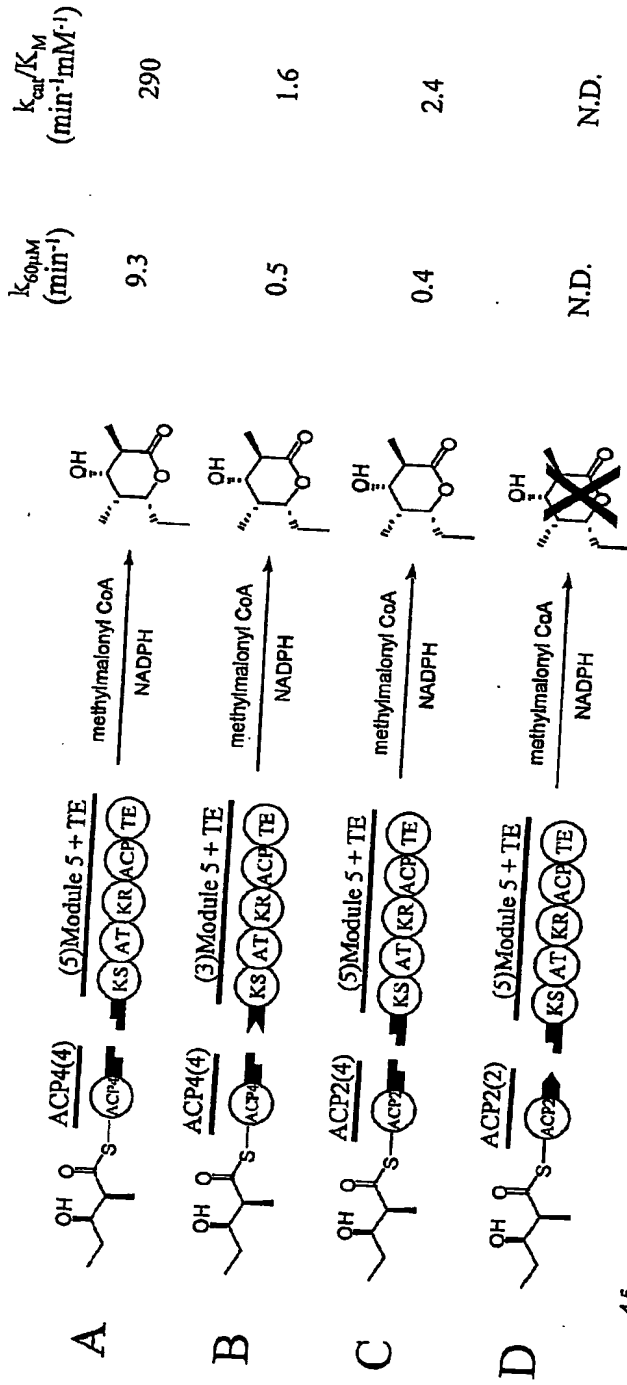


Figure 28

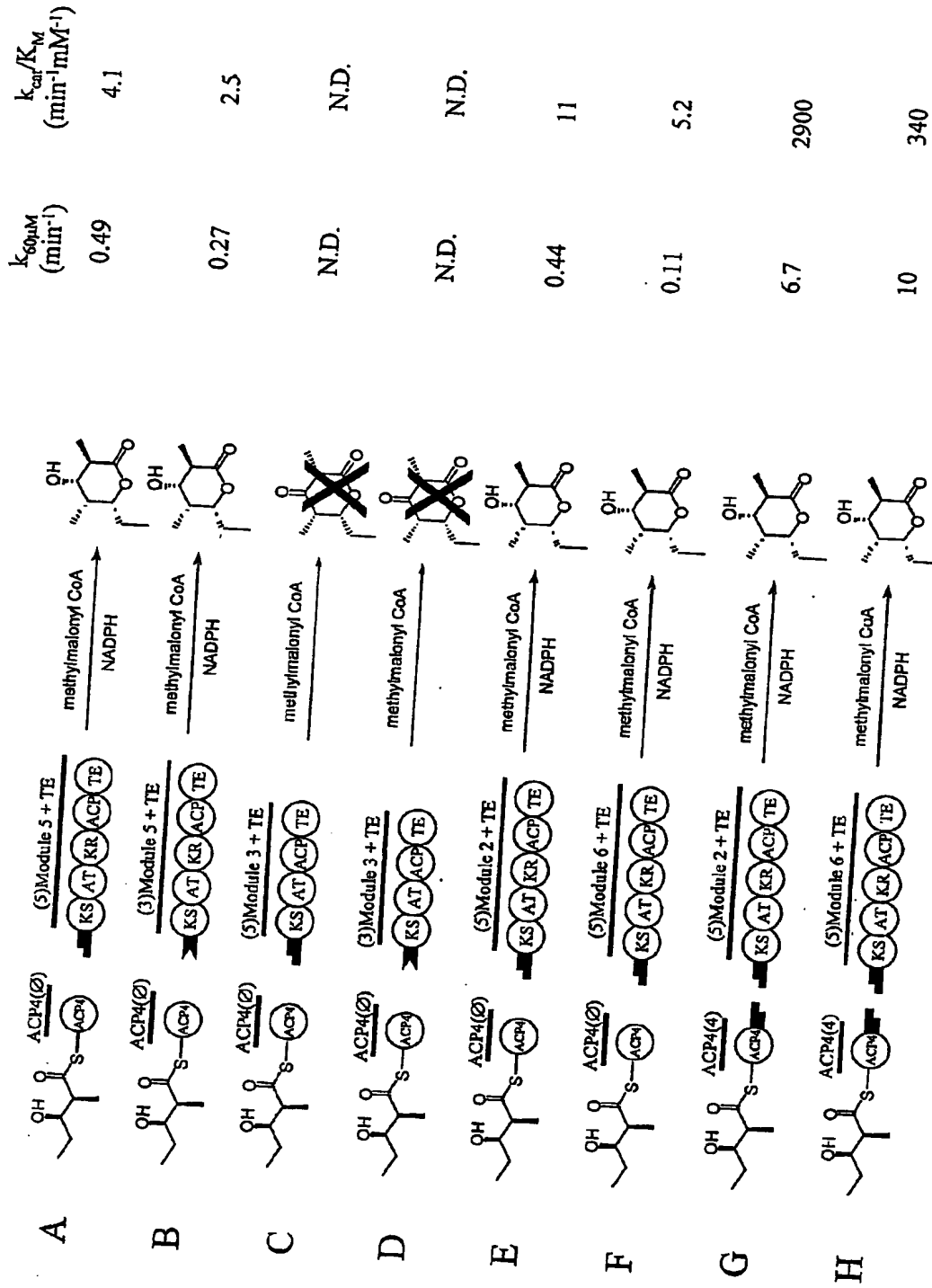


Figure 29

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A

ACP2(0)		✓	✓
eryLDD(0)		✓	✓
NovH(0)		X	X
NovH(4)		✓	✓

(5)Module 2 + TE	
(5)Module 6 + TE	

B

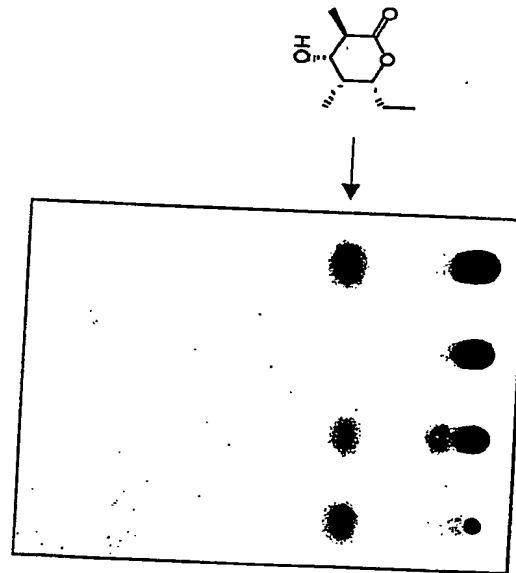


Figure 30

1	AAPOH VAVV	AMACRLEGGV	STDE	SEGRDAVAGL	PTGMDLOS	LTFEDPTREG	TABRGOGCH	TEATA	TPH	PNSEERRLA	MOHCLNTE	- 600
2	APVDS	I-I	GMA-L	EV DS	TSGRDSAAEV	-D	VPDE	IMASD....A	AGTRAH-HE	AG-GD	AA	-2071
3	ELES	I-I	SHA-L	GV NT	REGGETLSEF	-A	DLAR	LEHEDPDEPG	TSYVOK-GE	DD-AG	AE	- 126
4	ADSES	I-I	GIG-F	GI GS	AEGANI/TGP	-A	DIGR	LYHEDPDEPG	TSYVOK-GE	DD-AG	AE	-1584
5	BRAGE	I-I	GMA-F	DV DS	SGGDAIAEA	-A	EPD	PDARL-GH	AA-GD	AG	- 122
6	BRAGE	I-I	GMA-F	GV HE	VGRDAVTEH	-A	DLOA	LFOPDPREG	TSYSRH-HE	DG-AL	AA	-1581
1	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 700
2	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-2171
3	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 225
4	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-1684
5	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 222
6	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-1680
1	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 800
2	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-2271
3	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 325
4	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-1784
5	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 322
6	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-1780
1	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 898
2	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-2371
3	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 425
4	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-1882
5	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	- 422
6	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	IS-VL	-1880
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 992
2	RE-EPN	RE-EPN	RE-EPN	RE-EPN	RE-EPN	RE-EPN	RE-EPN	RE-EPN	RE-EPN	RE-EPN	RE-EPN	-2469
3	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 518
4	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-1974
5	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 515
6	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-1978
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 106
2	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-1089
3	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2559
4	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 612
5	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2066
6	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 603
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2068
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 204
2	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-1184
3	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2659
4	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 710
5	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2164
6	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 701
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2166
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 303
2	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-1284
3	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2758
4	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 809
5	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2263
6	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 800
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2265
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 388
2	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-1381
3	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2853
4	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 906
5	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2358
6	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 898
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2355
1	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-1439
2	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2908
3	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 957
4	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2592
5	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	- 952
6	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	EPN	-2399

Figure 31 A

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1ALESA GARVRELVD ARCGRDELAE BIRSV.GE.V AGVLSLLAVD EAFERAPLA LASLADTSLVOAMVSA ELCCPLW...	-1516
2ALARA -A.....E FEVTRG.VGG LVGDCA.....G-V-LIALE GD.....GAVQTLVVRELDAS GIDAPLW...	-2964
3ALERN -GRALCEVD TSASRTENAG AVAQAGT.GF RG-L-LISSD ESACR..PGV PAGAVGLITVQALGDA GVDAPVW...	-1033
4	AMMTVTLHAS -ATSUR.VVA TPAGADAMAL RVTPAGHIV AT-D-LVRS TGEWROPEP RGCGSLHADNGRIAEFGS TGRVVAADAS DLDVLRSGE	-2691
5GLEQS -ATVLTCDVESRSTIGT ALBAADTAL ST-V-LISRD GEADV..PSL DA.....LAVQALGAA GVEAPLW...	-1021
6AVEKA -GRV...VPV ASADREASA .LREVP.GEV AG-L-V.....HTCAATHLAHQSILGEA GVEAPLW...	-2459
1TVT ESAVATGPF EUREAARGAL WGVGVIALE KPAVWGGLVD VPAGSVARLA-1569	
2TV- FG-DAG.SP .VAREDOAKL W-LGQVASL RGRSTGLV LPHEPDPELR-3015	
3	FEPPAVLVRY EPGGDEPRAA ARHGVLWAAA LVRRMLEQEE LFGATLVIASG-TVSDD SVPEFGAARM W-VIRCAQA SPDRF.VLL TDAREFG...	-1086
4LV- RN-QUADGE LV.DPAQAMV G-LGRVVGI QPGRWGGLV LVDA.DAASI-2786	
5LV- SR-ALGESE .FVDFEQAMV W-LGRVVGI TPERWGGLV LPAPAPGCG-1072	
6LV- SR-ALGESE .FVDFEQAMV W-LGRVVGI TPERWGGLV LPAPAPGCG-2511	
1	RHLAAVVGSG A.GEDQLALR ADGVYGRWV NAAAPA	TIDE.WRGTG TULVVAOEG VGGGTHM ARBEPHML	-1642
2	GRIT-VLAG. .SEDOV-V- ADAVRAR-LS PAHVT.	ATSEYAV-G -I-V-EDAG VGGGTHM ARBEPHML	-1642
3	RILV-VLGG GRAEDHL-V- DGRLEGR-VV BASLPQ	SGSRMT-H -V-V-EDAG VGGGTHM ARBEPHML	-3086
4	MLP-V....PDPQL-L- GDDVEVP-LS FLAPSA	TOPASVD-D -V-V-EDAG VGGGTHM ARBEPHML	-1161
5	RLSL-VLAD PRGSESV-I- ADGIRVA-LV PAPARA	ARTR.MS-R -V-V-EDAG VGGGTHM ARBEPHML	-3171
6	EAPV-CIGAD G.BEDOV-I- DRARTGR-LV RAPLG.	TRESSME-A -A-V-EDAG VGGGTHM ARBEPHML	-1145
1	VSPGPDADG AGEVVAELEA RPARTVAAC FVDRSVRE BLOGI.GDOV HILSAVFAHA	TLDGGT.DTL TGERHPPSR ARBEPHML EDRELDLTA	-1741
2	VSPGPDADG VGD-TAELT- D-ARVSUR-C VESREPVRE LVHGLEGGD WPGVV-ARG	LPQVADMDH DEARDEWVA M-AGGAVED	-3184
3	VSPGPDADG GDD-LAVER DEASAVVC-D PWA...LRE ILGDE....FVVALV-RET	LTFEGUSEV APPEFAEDIA M-AGGAVED	-1248
4	VSPGPDADG SDE-RATED PASADIA-C TUDRDLSEA BLDGL...FR HILGVV-ARG	VLADGIMTSI DEPAVSCVLR M-AGGAVED	-3268
5	VSPGPDADG ASE-REBLTA HGTGVITA-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-1243
6	VSPGPDADG AAE-EAELVA H-ARTIT-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-2680
1	VSPGPDADG AAE-EAELVA H-ARTIT-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-1839
2	VSPGPDADG AAE-EAELVA H-ARTIT-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-3283
3	VSPGPDADG AAE-EAELVA H-ARTIT-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-1344
4	VSPGPDADG AAE-EAELVA H-ARTIT-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-3366
5	VSPGPDADG AAE-EAELVA H-ARTIT-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-1341
6	VSPGPDADG AAE-EAELVA H-ARTIT-C VDRARLEA VLAARAEGR TVSAVH-ARG	VSTSTHDDL TEARETHAD VGGGTHM ARBEPHML	-2777
1	RFLAYTAQR PTHLEHIDD ARRAA...EQ APAEPVGA. LASLPAPERE EALFELVREN	G REBDAETER STZIDEMAR CUSASAAI	-461
2	AFAESYT-AR PREHLDRIVT .TAPSERAG EPETESLIRD L-GLPRAERT AB-VRLVRS	T-TVL-HDDP KAVRATTF-K	-1935
3	VISEGFA-TR PTHLSAELAG RGGOAEASD SGPTCEPAQR L-GLSPDEQQ EN-LELVANA	VENL-HESA AELNVRA-S	-3381
4	ALR...R-EP VPEVIRGMVR AKILRAAGQAE A.AGPNVVDL L-GRSESDQV AG-RELVRSH	M-AMS-YGSA DQDPERRA-K	-1444
5	REVELET-AR HRELEDEIAG ARAEA...RQ SEEGPALAQR L-ALSTAERT EN-ABLIRAE	V-AMH-EGDD AMEDDRA-R	-3462
6	APAVGT-AR PREHLDRIVTPAGVAVFV O-APAREMTS OE-LEPTESH	V-AMH-EGDD AMEDDRA-R	-1437
1	GREVNALLY DEPTFRAIE ALAAG-2866	
2	-VRIPTITVF D--DVRTI-A HLAADGGAT GAQQAAPATT-486	
3	-LREPSLTV D--WASAV-G FLDAE-GTEV RG.EAFSA-1975	
4	-LREPSLTV D--TVTAI-Q HILRAV-VG..DADQAVRVV GA-3418	
5	-VRIPTITVF D--TFLAV-S HILROR-PAAS PAVDIGNRDL ELE-1484	
6	-LREPSLTV D--TITRI-D HILROR-VGAA EAEQAPALVR EYP-3505	
1	-LREPSLTV E--TVERI-D HIGG-DSGT PAREASSAIR DGY-1480	
2-2909		

Figure 31 B

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